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B3
cont

--146. (New) An adipose-derived lattice comprising adipose tissue extracellular matrix substantially devoid of cells. --

REMARKS

Claims 1-7 were pending in the subject application. Applicants have amended claims 1-4, and added new claims 139-146 above. Accordingly, claims 1-4 and 139-146 are pending.

Support for amended claims 1-4 are found in the specification as originally filed, and therefore do not involve new matter. Entry of these claims is respectfully requested.

Support for the amendment of claim 1 can be found in the originally-filed specification at the following:

Adipose-derived stem cell: page 2, line 26

Substantially free of adipocytes: page 2, lines 26-29; page 3, lines 31-37; and Example 1 at page 17, lines 19-37 and continuing at page 18, lines 1-3.

Substantially free of other cell types: page 2, lines 26-29

Pluripotent stem cell: page 2, lines 33-36; page 3, lines 1-23

Enriched for multipotent cells: page 4, lines 24-27

Clonally propagated stem cell: page 5, lines 17-34; page 8, lines 3-4 and lines 11-14; and Example 3 at page 19, lines 32-37 and continuing at page 20, lines 1-11.

Differentiates into at least two phenotypes: page 3, lines 14-23

Support for the amendment of claim 2 can be found in the originally-filed specification at the following:

Substantially homogenous: page 2, lines 26-29; page 3, lines 31-32; page 4, lines 24-27; and Example 1 at page 17, lines 19-37 and continuing at page 18, lines 1-3.

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Support for the amendment of claim 3 can be found in the originally-filed specification at page 4, lines 35-37 and continuing at page 5, lines 1-4.

Support for the amendment of claim 4 can be found in the originally-filed specification at page 2, lines 30-31.

Support for new claim 139 can be found in the originally-filed specification at page 2, lines 34-37; page 3, lines 1-23.

Support for new claim 140 can be found in the originally-filed specification at page 3, lines 14-19.

Support for new claim 141 can be found in the originally-filed specification at page 3, lines 14-19.

Support for new claim 142 can be found in the originally-filed specification at page *Fraction*: page 3, lines 31-37 and continuing at page 4, lines 1-27; Example 1 at page 17, lines 19-37, and continuing at page 18, lines 1-3.

Clonally propagated: page 5, lines 17-34; page 8, lines 3-4 and lines 11-14; and Example 3 at page 19, lines 32-37 and continuing at page 20, lines 1-11.

Enriched for multipotent cells: page 4, lines 24-27.

3 different phenotypes: page 3, lines 14-23

Support for new claim 143 can be found in the originally-filed specification at page 3, lines 14-19.

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Support for new claims 144 and 145 can be found in the originally-filed specification at page 3, lines 14-23; lines 31-37 and continuing at page 4, lines 1-27; Example 1 at page 17, lines 19-37 and continuing at page 18, lines 1-3.

Support for new claim 146 can be found in the originally-filed specification at page 2, line 5, lines 12-14; page 14, lines 20-37; page 15, lines 1-9; Example 6 at page 21, lines 27-37 and continuing at page 22, lines 1-9.

In view of the changes to the claims and the remarks which follow, Applicants respectfully request reconsideration of the outstanding rejections and objections to the claims.

APPLICANTS' INVENTION

The present invention provides a multipotent stem cell isolated from adipose tissue (e.g., the adipose-derived stem cell of the invention). The present invention also provides a substantially homogenous population of adipose-derived stem cells. The isolated adipose stem cell, and the homogenous population, is substantially free of adipocytes and red blood cells.

Under different culture conditions, the adipose-derived stem cells of the invention can differentiate into cell types of ectodermal, mesodermal and/or endodermal lineage. The claimed stem cells can differentiate into at least two types of cells having different developmental phenotypes, including: adipogenic, chondrogenic, cardiogenic, dermatogenic, hematopoietic, hemangiogenic, myogenic, nephrogenic, neurogenic, neuralgiogenic, urogenitogenic, osteogenic, pericardiogenic, peritoneogenic, pleurogenic, splanchnogenic, and stromal.

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The adipose-derived stem cells of the invention can be maintained in culture in an undifferentiated state. For example, the stem cells can be passaged at least 15 times without differentiating.

The present invention also provides adipose-derived lattices comprising extracellular matrix of adipose tissue. The lattices are substantially free of cells. Additionally, the present invention provides methods for isolating the adipose-derived stem cell, the substantially homogenous population, and the adipose-derived lattices.

REJECTIONS UNDER 35 U.S.C. 112, SECOND PARAGRAPH

In paragraphs 2-3, the Patent Office rejected claims 1-4 as allegedly indefinite because the term “substantially free of mature adipocytes” is not defined in the specification or claims.

Applicants respectfully disagree. The term “substantially free of mature adipocytes” is supported in the originally-filed specification at: page 2, lines 26-29; page 3, lines 31-37; and Example 1 at page 17, lines 19-37 and continuing at page 18, lines 1-3. Accordingly, Applicants respectfully request that the Patent Office withdraw this rejection.

REJECTIONS UNDER 35 U.S.C. 101

In paragraphs 4-5, the Patent Office rejected claims 1-4 as allegedly directed to non-statutory subject matter. In response, applicants have amended the claims to recite an “isolated” cell. Accordingly, the rejection is now moot.

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REJECTIONS UNDER 35 U.S.C. 102

In paragraphs 6-9, the Patent Office rejected claims 1-4 as allegedly anticipated under 35 U.S.C. §102(b) in view of various references. Applicants respectfully traverse these rejections. These references do not disclose each and every element of the claimed invention in a manner sufficient to enable one skilled in the art to reduce the invention to practice.

Paragraphs 6-7

In paragraphs 6-7, the Patent Office rejected claim 1 as allegedly anticipated under 35 U.S.C. §102(b) by U.S. Patent No. 5,486,359 ('359 patent), U.S. Patent No. 5,728,739 ('739 patent), Ailhaud et al. (1983) and Vassaux et al. (of record).

'359 Patent

The '359 patent teaches mesenchymal stem cells having a potential for differentiating into a variety of cells having phenotypes all within the **mesodermal** germ line. The '359 patent teaches that the source of mesenchymal stem cells are blood, bone marrow, dermis (column 1, lines 45-47) and embryonic yolk sac, placenta umbilical cord fetal and adolescent skin, and blood (column 2, lines 18-21).

The '359 patent does not teach the claimed multipotent stem cells derived from adipose tissue or a population of these stem cells. The claimed adipose-derived stem cell can differentiate into cells of the mesodermal, endodermal and ectodermal lineages. Since the '359 patent does not teach each and every element of the isolated adipose-derived stem cell as claimed, the teachings in '359 cannot anticipate the claimed stem cells.

‘739 Patent

The ‘739 patent teaches compounds that induce preadipocytes to differentiate into mature adipocytes. However, ‘739 does not teach the claimed adipose-derived stem cells, or a population of these stem cells, which can differentiate into at least two types of cells having different developmental phenotypes (e.g., multipotent stem cells). Since the ‘739 patent does not teach each and every element of the isolated adipose-derived stem cell as claimed, the teachings in ‘739 cannot anticipate the claimed stem cells.

Ailhaud et al (1983)

Ailhaud et al (1983) teaches methods for culturing an established preadipocyte cell line, ob17, to induce differentiation into mature adipocytes. However, Ailhaud (1983) does not teach adipose-derived stem cells which are multipotent. Since Ailhaud (1983) does not teach each and every element of the claimed isolated adipose-derived stem cell, or a population of the claimed stem cells, the teachings in this reference cannot anticipate the claimed stem cells.

Vassaux et al.

Vassaux et al. teaches an adipose precursor cells which develop into mature fat cells. However, Vassaux does not teach adipose-derived stem cells which are multipotent. Since Vassaux does not teach each and every element of the isolated adipose-derived stem cell as claimed, or a population of these stem cells, the teachings in this reference cannot anticipate the claimed stem cells.

Paragraph 8

In paragraph 8, the Patent Office rejected claims 1-3 as allegedly anticipated under 35 U.S.C. §102(b) by each of Ailhaud et al. (1985) and Marko et al. (of record), and Soda et al.

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Ailhaud et al. (1985)

This reference is published in a French scientific journal having an English-language Summary. Ailhaud (1985) teaches methods for culturing an established preadipocyte cell line, ob17, to induce differentiation into mature adipocytes. However, Ailhaud (1985) does not teach adipose-derived stem cells which are multipotent. Since Ailhaud (1985) does not teach each and every element of the isolated adipose-derived stem cell as claimed, or a population of these stem cells, the teachings in this reference cannot anticipate the claimed stem cells.

Marko et al

Marko et al., teaches methods for isolating preadipocytes from bone marrow. However, Marko does not teach multipotent stem cells which are derived from adipose tissue. Since Marko does not teach each and every element of the claimed isolated adipose-derived stem cell as claimed, or a population of these stem cells, the teachings in this reference cannot anticipate the claimed stem cells.

Soda et al.

Soda is a review article that teaches isolated adipose tissue that can be cultured to differentiate into mature adipocytes. However, Soda does not teach adipose-derived stem cells that are multipotent. Since Soda does not teach each and every element of the isolated adipose-derived stem cell as claimed, the teachings in this reference cannot anticipate the claimed cells.

Paragraph 9

In paragraph 9, the Patent Office rejected claims 1-4 as allegedly anticipated under 35 U.S.C. §102(b) by WO 98/04682 (of record).

WO 98/04682 teaches mesenchymal stem cells isolated from bone marrow which can differentiate into adipocytes. However, WO 98/04682 does not teach the claimed adipose-derived stem cells that are multipotent. Since this reference does not teach each and every element of the isolated adipose-derived stem cell as claimed, or a population of these stem cells, the teachings in this reference cannot anticipate the claimed cells.

Paragraph 10

In paragraph 10, the Patent Office rejected claim 1 as allegedly anticipated under 35 U.S.C. §102(e) by U.S. Patent No. 5,854,292 ('292 patent) and U.S. Patent No. 5,827,897 ('897 patent) (of record).

'292 Patent

The '292 patent teaches compounds that induce preadipocytes to differentiate into mature adipocytes. However, '292 does not teach the claimed adipose-derived stem cells which can differentiate into at least two types of cells having different developmental phenotypes (e.g., multipotent stem cells), or a population of these cells. Since the '292 patent does not teach each and every element of the isolated adipose-derived stem cell as claimed, the teachings in this reference cannot anticipate the claimed cells.

'897 Patent

The '897 patent teaches compounds that induce preadipocytes to differentiate into mature adipocytes. However, '897 does not teach the claimed adipose-derived stem cells which can differentiate into at least two types of cells having different developmental phenotypes (e.g., multipotent stem cells), or a population of these cells. Since the '897

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patent does not teach each and every element of the isolated adipose-derived stem cell as claimed, the teachings in '897 cannot anticipate the claimed cells.

Paragraph 11

In paragraph 11, the Patent Office rejected claims 1-4 as allegedly anticipated under 35 U.S.C. §102(e) by U.S. Patent No. 5,827,740 ('740 patent) (of record).

The '740 patent teaches mesenchymal stem cells isolated from bone marrow which can differentiate into adipocytes. However, '740 does not teach the claimed adipose-derived stem cells that are multipotent, or a population of these cells. Since this reference does not teach each and every element of the isolated adipose-derived stem cell as claimed, the teachings in this reference cannot anticipate the claimed cells.

CONCLUSION

In view of the Applicants' above amendments and responses to the Patent Office's rejection of the claims of the subject application, Applicants contend that the subject application is in condition for allowance. Accordingly, Applicants request issuance of a Notice of Allowance.

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Only the fee for a two-month extension of time is deemed necessary in connection with the filing of this Amendment. The fee for the two-month extension of time is \$200.00. A check for \$200.00 is enclosed. If any additional fee is necessary, the Patent Office is authorized to charge any additional fee to Deposit Account No. 50-0306.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE IN THE CLAIMS

- 1. (Amended) An isolated adipose-derived stem cell can differentiate into two or more developmental phenotypes selected from the group consisting of adipogenic, chondrogenic, cardiogenic, dermatogenic, hematopoetic, hemangiogenic, myogenic, nephrogenic, neurogenic, neuralgiogenic, urogenitogenic, osteogenic, pericardiogenic, peritoneogenic, pleurogenic, splanchnogenic, and stromal developmental phenotypes [A mammalian lipo-derived stem cell substantially free of mature adipocytes]. --
- 2. (Amended) A substantially homogeneous population of adipose-derived stem cells, comprising a plurality of the stem cell of claim 2 [The cell of claim 1, which can be cultured in DMEM + about 10% fetal bovine serum for at least 15 passages without differentiating]. --
- 3. (Amended) The adipose-derived stem cell of claim 1 or the population of claim 2 which can be cultured for at least 15 passages without differentiating. [The cell of claim 2, which has two or more developmental phenotypes selected from the group of developmental phenotypes consisting of adipogenic, chondrogenic, cardiogenic, dermatogenic, hematopoetic, hemangiogenic, myogenic, nephrogenic, neurogenic, neuralgiogenic, urogenitogenic, osteogenic, pericardiogenic, peritoneogenic, pleurogenic, splanchnogenic, and stromal developmental phenotypes]. --
- 4. (Amended) The adipose-derived stem cell of claim 1 or the population of claim 2 which is human [The cell of any of claims 1-3 which is human]. --